Title: Cystic Fibrosis and Congenital Absence of the Vas Deferens *GeneReview* – Specifics of diagnostic tests
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Note: The following information is provided by the authors listed above and has not been reviewed by *GeneReviews* staff.

Quantitative Pilocarpine Iontophoresis Sweat Chloride

Accurate performance of the sweat chloride test is critical for the diagnosis of CF. The US CF Foundation requires that sweat chloride testing be conducted at accredited CF Centers, adhering to standards set by the CF Foundation, in accordance with guidelines provided by the Clinical Laboratory Standards Institute [Clinical Laboratory Standards Institute 2000, LeGrys et al 2007].

- A minimum sweat weight of 75 mg must be collected during a 30-minute period to assure a sweat rate of 1 g/M^2/min.
- A chloride concentration greater than 60 mEq/L in sweat on two separate occasions is diagnostic.

Note: (1) Sweat chloride levels higher than 160 mEq/L are not physiologically possible and should be attributed to technical error. (2) Elevated sweat chloride results may also be caused by malnutrition, other disorders (e.g., mucopolysaccharidosis type 1 (Hurler syndrome), pseudohypoaldosteronism, hypoparathyroidism, fucosidosis, nephrogenic diabetes insipidus, ectodermal dysplasia, atopic dermatitis, and adrenocorticoid deficiency), certain medications [Feldshtein et al 2010, Guglani et al 2012] and arsenic poisoning [Mazumdar et al 2015]. (3) False negative sweat chloride results may occur in the setting of acute CF-related salt losses. (4) When CF is suspected in an individual with hyponatremia and hypochloremia, sweat testing should be deferred until electrolyte balance has been restored and fluid status stabilized. (5) When the sweat test is in the intermediate range (30-59 mmol/L) DNA analysis may be able to establish the diagnosis.

Transepithelial Nasal Potential Difference (NPD)

Respiratory epithelia regulate ion transport and alter content of the airway surface fluid by active transport mechanisms. The absence of functional CFTR at the apical surface with resultant alterations in chloride efflux and sodium transport produces an abnormal electrical potential difference across epithelial surfaces. The protocol for NPD measurements in individuals older than age six years is well described, standardized, and safely performed in many specialized CF centers worldwide [Schüler et al 2004, Standaert et al 2004].

Individuals with CF have the following:

- A raised (more negative) baseline NPD reflecting enhanced sodium absorption across a relatively chloride-impermeable membrane

- A greater change in NPD during perfusion of the nasal mucosa with amiloride, an inhibitor of sodium channel activity
- Minimal change in NPD in response to perfusion with amiloride/low chloride/beta-agonist, as a measure of cAMP-mediated chloride transport via CFTR

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